

MGLM: An R Package for Multivariate Categorical Data Analysis

by Juhyun Kim, Yiwen Zhang, Joshua Day, Hua Zhou

Abstract Data with multiple responses is ubiquitous in modern applications. However, few tools are available for regression analysis of multivariate counts. The most popular multinomial-logit model has a very restrictive mean-variance structure, limiting its applicability to many data sets. This article introduces an R package **MGLM**, short for multivariate response generalized linear models, that expands the current tools for regression analysis of polytomous data. Distribution fitting, random number generation, regression, and sparse regression are treated in a unifying framework. The algorithm, usage, and implementation details are discussed.

Introduction

Multivariate categorical data arises in many fields, including genomics, image analysis, text mining, and sports statistics. The multinomial-logit model (Agresti, 2002, Chapter 7) has been the most popular tool for analyzing such data. However, it is limiting due to its specific mean-variance structure and the strong assumption that the counts are negatively correlated. Models that address over-dispersion relative to a multinomial distribution and incorporate positive and/or negative correlation structures would offer greater flexibility for analysis of polytomous data.

In this article, we introduce an R package **MGLM**, short for multivariate response generalized linear models. The **MGLM** package provides a unified framework for random number generation, distribution fitting, regression, hypothesis testing, and variable selection for multivariate response generalized linear models, particularly four models listed in Table 1. These models considerably broaden the class of generalized linear models (GLM) for analysis of multivariate categorical data.

MGLM overlaps little with existing packages in R and other softwares. The standard multinomial-logit model is implemented in several R packages (Venables and Ripley, 2002) with **VGAM** (Yee, 2010, 2015, 2017) being the most comprehensive. We include the classical multinomial-logit regression model in **MGLM** not only for completeness, but also to complement it with various penalty methods for variable selection and regularization. If invoked by the group penalty, **MGLM** is able to perform variable selection at the predictor level for easier interpretation. This is different from the elastic net penalized multinomial-logit model implemented in **glmnet** (Friedman et al., 2010), which does selection at the matrix entry level. Although **MGLM** focuses on regression, it also provides distribution fitting and random number generation for the models listed in Table 1. **VGAM** and **dirmult** (Tvedebrink, 2010) packages can estimate the parameters of the Dirichlet-multinomial (DM) distribution using Fisher's scoring and Newton's method respectively. As indicated in the manual (Yee, 2017), the convergence of Fisher's scoring method may be slow due to the difficulty in evaluating the expected information matrix. Further the Newton's method is unstable as the log-likelihood function may be non-concave. As explained later, **MGLM** achieves both stability and efficiency via a careful algorithmic design. In SAS, PROC LOGISTIC can fit multinomial-logit model. In Matlab, the `mnrfit` function fits multinomial-logit regression. Alternative link functions (probit, loglog, complementary loglog) are implemented only for ordinal responses. Other regression models in Table 1 are not implemented in either SAS or Matlab.

There are some limitations to the **MGLM**. First, **MGLM** only handles nominal responses; ordinal responses are not incorporated in current implementation. **MGLM** also does not allow covariates to take a different value for each category, which can be useful in applications such as modeling consumer choice among a discrete number of products (Yee, 2015, Chapter 14). Lastly, current implementation of **MGLM** does not permit parameter constraints.

MGLM provides standard errors for all estimates, reports significance of regression covariates based on the Wald test (default) or the likelihood ratio test (LRT), and outputs the AIC (Akaike information criterion) and BIC (Bayesian information criterion) of the fitted model to aid model choice by users. Model selection via regularization is automated by computing the solution path on a grid of tuning parameter values and then reporting the regularized estimate with minimal BIC. With large data sets in mind, we pay particular attention to computational efficiency. For numerical examples in this article, we report the run times whenever possible. The results are obtained on a laptop with Intel Core i7 CPU @ 2.9GHz and 16G memory using **MGLM** 0.1.0 under R 3.4.3.

Model	No. regress. param.	Correlation	MGLM code
Multinomial	$p(d-1)$	Negative	dist='MN'
Dirichlet-multinomial	pd	Negative	dist='DM'
Negative multinomial	$p(d+1)$ or $pd+1$	Positive	dist='NegMN'
Gen. Dirichlet-multinomial	$2p(d-1)$	Negative and positive	dist='GDM'

Table 1: Multivariate generalized linear model implemented in the **MGLM** package. d is the number of categories and p is the number of predictors in the regression model.

Multivariate generalized linear models (MGLM)

This section details the models implemented in **MGLM**. Table 1 summarizes the multivariate models implemented in the R package. They are multivariate analogs of binomial, beta-binomial, and negative binomial models. For each model, we specify the probability mass function of the response vector \mathbf{y} , the link function that relates distribution parameters to covariates, and the log-likelihood function of a finite sample. We start from the classical multinomial-logit model.

Multinomial (MN) model

The probability mass function of a d dimensional multinomial sample $\mathbf{y} = (y_1, \dots, y_d)^T$ with batch size $m = \sum_{j=1}^d y_j$ and parameter $\mathbf{p} = (p_1, \dots, p_d)$ is

$$f(\mathbf{y}|\mathbf{p}) = \binom{m}{\mathbf{y}} \prod_{j=1}^d p_j^{y_j}.$$

The parameter \mathbf{p} is linked to the covariate vector $\mathbf{x} \in \mathbb{R}^p$ via the multinomial-Poisson transformation (Baker, 1994; Lang, 1996)

$$p_j = \frac{e^{\mathbf{x}^T \boldsymbol{\beta}_j}}{\sum_{j'} e^{\mathbf{x}^T \boldsymbol{\beta}_{j'}}}, \quad j = 1, \dots, d,$$

where $\boldsymbol{\beta}_1, \dots, \boldsymbol{\beta}_d \in \mathbb{R}^p$ are the regression coefficients. For identifiability, we constrain $\boldsymbol{\beta}_d = \mathbf{0}$ and only estimate $\boldsymbol{\beta}_1, \dots, \boldsymbol{\beta}_{d-1}$, which are collected in the regression coefficient matrix $\mathbf{B} \in \mathbb{R}^{p \times (d-1)}$. Given independent observations $(\mathbf{y}_i, \mathbf{x}_i)$, $i = 1, \dots, n$, the log-likelihood is

$$\ell(\mathbf{B}) = \sum_{i=1}^n \sum_{j=1}^d y_{ij} \left(\mathbf{x}_i^T \boldsymbol{\beta}_j - \ln \sum_{j'=1}^d e^{\mathbf{x}_i^T \boldsymbol{\beta}_{j'}} \right) + \sum_{i=1}^n \ln \binom{m_i}{\mathbf{y}_i}.$$

Because the log-sum-exponential mapping $(\eta_1, \dots, \eta_d)^T \mapsto \ln \sum_j e^{\eta_j}$ is convex (Boyd and Vandenberghe, 2004, p72), the log-likelihood function is concave. This nice feature makes maximum likelihood estimation relatively easy for multinomial-logit model. Unfortunately, convexity is lost in other models listed in Table 1.

Dirichlet-multinomial (DM) model

The mean-variance structure of the MN model does not allow over-dispersion, which is common in real data. DM distribution models the probability parameter \mathbf{p} in the MN model by a Dirichlet distribution. The probability mass of a d -category count vector \mathbf{y} over $m = \sum_j y_j$ trials under DM with parameter $\boldsymbol{\alpha} = (\alpha_1, \dots, \alpha_d)$, $\alpha_j > 0$ and proportion vector $\mathbf{p} \in \Delta_d = \{(p_1, \dots, p_d) : p_j \geq 0, \sum_j p_j = 1\}$ is

$$\begin{aligned}
 f(\mathbf{y}|\boldsymbol{\alpha}) &= \int_{\Delta_d} \binom{m}{\mathbf{y}} \prod_j p_j^{y_j} \frac{\Gamma(\sum_j \alpha_j)}{\prod_j \Gamma(\alpha_j)} \prod_j p_j^{\alpha_j - 1} d\mathbf{p} \\
 &= \binom{m}{\mathbf{y}} \prod_{j=1}^d \frac{\Gamma(\alpha_j + y_j)}{\Gamma(\alpha_j)} \frac{\Gamma(\sum_j \alpha_j)}{\Gamma(\sum_j \alpha_j + \sum_j y_j)} \\
 &= \binom{m}{\mathbf{y}} \frac{\prod_{j=1}^d (\alpha_j)_{y_j}}{(\sum_j \alpha_j)_m},
 \end{aligned}$$

where $(a)_k = a(a + 1) \cdots (a + k - 1)$ for nonnegative integer k denotes the rising factorial. The last equality is due to the identity $\Gamma(a + k)/\Gamma(a) = (a)_k$ (Graham et al., 1994). Because the data y_j and parameter α_j are intertwined in the gamma (or rising factorial) terms and do not factorize, the DM distribution does *not* belong to the exponential family. To incorporate covariates, the inverse link function

$$\alpha_j = e^{\mathbf{x}^T \boldsymbol{\beta}_j}, \quad j = 1, \dots, d$$

relates the parameter $\boldsymbol{\alpha} = (\alpha_1, \dots, \alpha_d)$ of the DM distribution to the covariates \mathbf{x} . The log-likelihood for independent data points $(\mathbf{y}_i, \mathbf{x}_i), i = 1, \dots, n$, takes the form

$$\ell(\mathbf{B}) = \sum_{i=1}^n \sum_{j=1}^d \sum_{k=0}^{y_{ij}-1} \ln(e^{\mathbf{x}_i^T \boldsymbol{\beta}_j} + k) - \sum_{i=1}^n \sum_{k=0}^{m_i-1} \ln\left(\sum_{j=1}^d e^{\mathbf{x}_i^T \boldsymbol{\beta}_j} + k\right) + \sum_{i=1}^n \ln\binom{m_i}{\mathbf{y}_i}$$

with $\mathbf{B} = (\boldsymbol{\beta}_1, \dots, \boldsymbol{\beta}_d) \in \mathbb{R}^{p \times d}$ collecting all regression coefficients. The log-likelihood, as a difference of two convex terms, is not concave in general.

Negative multinomial (NegMN) model

The counts Y_j in both MN and DM models are negatively correlated, restricting their use for counts with positive correlation. The NegMN distribution provides a natural model for positively correlated count data. The probability mass of a count vector \mathbf{y} under a NegMN distribution with parameter $(p_1, \dots, p_{d+1}, \phi), \sum_{j=1}^{d+1} p_j = 1, p_j, \phi > 0$, is

$$f(\mathbf{y}|\mathbf{p}, \phi) = \binom{\phi + m - 1}{m} \binom{m}{\mathbf{y}} \prod_{j=1}^d p_j^{y_j} p_{d+1}^\phi = \frac{(\phi)_m}{m!} \binom{m}{\mathbf{y}} \prod_{j=1}^d p_j^{y_j} p_{d+1}^\phi$$

where $\binom{\phi + m - 1}{m} = \frac{(\phi)_m}{m!}$ is the general binomial coefficient. The parameter ϕ and the data m do not factorize. Therefore, NegMN does *not* belong to the exponential family when ϕ is unknown. We use the inverse link functions

$$p_j = \frac{e^{\mathbf{x}^T \boldsymbol{\alpha}_j}}{1 + \sum_{j=1}^d e^{\mathbf{x}^T \boldsymbol{\alpha}_j}}, 1 \leq j \leq d, \quad p_{d+1} = \frac{1}{1 + \sum_{j=1}^d e^{\mathbf{x}^T \boldsymbol{\alpha}_j}}, \quad \phi = e^{\mathbf{x}^T \boldsymbol{\beta}}$$

to relate the covariates \mathbf{x} to distribution parameter $(p_1, \dots, p_{d+1}, \phi)$. Let $\mathbf{B} = (\boldsymbol{\alpha}_1, \dots, \boldsymbol{\alpha}_d, \boldsymbol{\beta}) \in \mathbb{R}^{p \times (d+1)}$ collect all the regression coefficients. Given n independent data points $(\mathbf{y}_i, \mathbf{x}_i), i = 1, \dots, n$, the log-likelihood is

$$\begin{aligned}
 \ell(\mathbf{B}) &= \sum_{i=1}^n \sum_{k=0}^{m_i-1} \ln(e^{\mathbf{x}_i^T \boldsymbol{\beta}} + k) - \sum_{i=1}^n (e^{\mathbf{x}_i^T \boldsymbol{\beta}} + m_i) \ln\left(\sum_{j=1}^d e^{\mathbf{x}_i^T \boldsymbol{\alpha}_j} + 1\right) \\
 &\quad + \sum_{i=1}^n \sum_{j=1}^d y_{ij} \mathbf{x}_i^T \boldsymbol{\alpha}_j - \sum_{i=1}^n \sum_{j=1}^d \ln y_{ij}!,
 \end{aligned}$$

which in general is not concave in $\boldsymbol{\alpha}_j$ and $\boldsymbol{\beta}$.

In some applications the over-dispersion parameter ϕ may not depend on the covariates \mathbf{x} . MGLM offers the option to model the responses y_i to share a common dispersion parameter ϕ , without linking it to the covariates. In this case, the log-likelihood is

$$\begin{aligned} \ell(\alpha_1, \dots, \alpha_d, \phi) &= \sum_{i=1}^n \sum_{k=0}^{m_i-1} \ln(\phi + k) - \sum_{i=1}^n (\phi + m_i) \ln \left(\sum_{j=1}^d e^{x_i^T \alpha_j} + 1 \right) \\ &\quad + \sum_{i=1}^n \sum_{j=1}^d y_{ij} x_i^T \alpha_j - \sum_{i=1}^n \sum_{j=1}^d \ln y_{ij}!. \end{aligned}$$

The model size is $pd + 1$ and **MGLM** outputs the estimates $(\hat{\alpha}_1, \dots, \hat{\alpha}_d, \hat{\phi})$ and their standard errors.

Generalized Dirichlet-multinomial (GDM) model

In the previous three models, the multivariate counts have either pairwise negative correlation (MN and DM) or pairwise positive correlation (NegMN). It is possible to relax these restrictions by choosing a more flexible mixing distribution for the probability vector \mathbf{p} in MN model. [Connor and Mosimann \(1969\)](#) suggest a generalization of the Dirichlet distribution that meets this challenge. The resulting admixed distribution, called the GDM distribution, provides a flexible model for multivariate categorical data with a general correlation structure ([Bouguila, 2008](#); [Zhou and Lange, 2010](#)).

The probability mass of a count vector \mathbf{y} over $m = \sum_j y_j$ trials under GDM with parameter $(\alpha, \beta) = (\alpha_1, \dots, \alpha_{d-1}, \beta_1, \dots, \beta_{d-1}), \alpha_j, \beta_j > 0$, is

$$\begin{aligned} f(\mathbf{y}|\alpha, \beta) &= \binom{m}{\mathbf{y}} \prod_{j=1}^{d-1} \frac{\Gamma(\alpha_j + y_j)}{\Gamma(\alpha_j)} \frac{\Gamma(\beta_j + z_{j+1})}{\Gamma(\beta_j)} \frac{\Gamma(\alpha_j + \beta_j)}{\Gamma(\alpha_j + \beta_j + z_j)} \\ &= \binom{m}{\mathbf{y}} \prod_{j=1}^{d-1} \frac{(\alpha_j)_{y_j} (\beta_j)_{z_{j+1}}}{(\alpha_j + \beta_j)_{z_j}}, \end{aligned} \tag{1}$$

where $z_j = \sum_{k=j}^d y_k$. Again it is clear that the GDM distribution does not belong to the exponential family, since the parameter α_j, β_j and data y_j, z_j do not factorize.

We propose the inverse link functions

$$\alpha_j = e^{x^T \alpha_j}, \quad \beta_j = e^{x^T \beta_j}, \quad 1 \leq j \leq d - 1,$$

to relate the covariates \mathbf{x} and parameter $(\alpha_1, \dots, \alpha_{d-1}, \beta_1, \dots, \beta_{d-1})$ of the GDM distribution (1). Let $\mathbf{B} = (\alpha_1, \dots, \alpha_{d-1}, \beta_1, \dots, \beta_{d-1}) \in \mathbb{R}^{p \times 2(d-1)}$ collect all the regression coefficients. Given n independent data points $(\mathbf{y}_i, \mathbf{x}_i)$, the log-likelihood is

$$\begin{aligned} \ell(\mathbf{B}) &= \sum_{i=1}^n \sum_{j=1}^{d-1} \left[\sum_{k=0}^{y_{ij}-1} \ln \left(e^{x_i^T \alpha_j} + k \right) + \sum_{k=0}^{z_{i,j+1}-1} \ln \left(e^{x_i^T \beta_j} + k \right) \right. \\ &\quad \left. - \sum_{k=0}^{z_{ij}-1} \ln \left(e^{x_i^T \alpha_j} + e^{x_i^T \beta_j} + k \right) \right] + \sum_{i=1}^n \ln \binom{m_i}{\mathbf{y}_i}. \end{aligned}$$

Again the log-likelihood is not concave in general.

Which model to use?

When there are no covariates, multinomial model is a special case of the DM models, which in turn is a sub-model of the GDM model. That is, $MN \subset DM \subset GDM$. The distribution fitting function **MGLMfit** reports the p -value of the LRT for comparing the fitted model with the most commonly used multinomial model. NegMN model does not have such a relationship with any of the other three models. Therefore, no LRT is performed when `dist="NegMN"` in the distribution fitting function **MGLMfit**.

For regression, there is no nesting structure among the models in [Table 1](#). The regression function **MGLMreg** outputs AIC and BIC of the fitted model to aid users in choosing an appropriate regression model for their data.

Standard errors and testing

Standard errors for both distribution fitting (MGLMfit) and regression estimates (MGLMreg) are calculated based on the observed information matrix, as it provides a reasonable approximation to the expected information matrix and is even preferred as argued by [Efron and Hinkley \(1978\)](#).

Unlike regression for univariate responses, the **MGLM** regression parameter is a matrix $\mathbf{B} = (\boldsymbol{\beta}_1, \dots, \boldsymbol{\beta}_{d_e}) \in \mathbb{R}^{p \times d_e}$ with each row $\mathbf{B}_{k\cdot}$, corresponding to the effects of one predictor. Here $d_e = d - 1$ (MN), d (DM), $d + 1$ (NegMN), or $2(d - 1)$ (GDM). Therefore, the hypotheses for testing the significance of the k -th covariate are:

$$H_0 : \|\mathbf{B}_{k\cdot}^T\|_2 = 0 \quad \text{vs} \quad H_a : \|\mathbf{B}_{k\cdot}^T\| \neq 0.$$

By default, MGLMreg assesses the significance of each predictor by the Wald test. Let

$$\widehat{\boldsymbol{\Sigma}} = \mathbf{I}_{\text{obs}}^{-1}(\widehat{\mathbf{B}}) = [-\nabla^2 \ell(\widehat{\mathbf{B}})]^{-1} \in \mathbb{R}^{pd_e \times pd_e}$$

be the inverse of the observed information matrix at the maximum likelihood estimate (MLE) $\widehat{\mathbf{B}}$. Then the Wald statistic is computed as

$$W_k = \widehat{\mathbf{B}}_{k\cdot} \widehat{\boldsymbol{\Sigma}}_{k,k} \widehat{\mathbf{B}}_{k\cdot}^T,$$

where $\widehat{\boldsymbol{\Sigma}}_{k,k}$ is the sub-matrix of $\widehat{\boldsymbol{\Sigma}}$ obtained by selecting rows and columns corresponding to the entries of $\widehat{\mathbf{B}}_{k\cdot}$. W_k is asymptotically distributed as a chi-square distribution with d_e degrees of freedom under the null distribution, yielding the p -values reported by MGLMreg. Users can also easily invoke the LRT by calling MGLMreg with option LRT=TRUE. LRT requires more computation than Wald test as it needs to perform MLE on p sub-models.

Regularization

The number of parameters, pd_e , in the multivariate response models can be unwieldy with a moderate to large number of predictors. When the sample size n is limited or even smaller than pd_e , regularization is necessary for variable selection, model interpretation, and improving the risk property of the estimate. In general, the MGLMsparse function solves the regularized problem

$$\min_{\mathbf{B}} -\ell(\mathbf{B}) + J(\mathbf{B}),$$

where ℓ is the log-likelihood function and J is a penalty term. The choice of J depends on specific applications. We implemented three classes of penalties. Below, \mathcal{S} is an index set for the set of predictors subject to regularization, which can be selectively specified by the users.

In *elementwise regularization* (penalty='sweep'),

$$J(\mathbf{B}) = \sum_{k \in \mathcal{S}} \sum_{j=1}^{d_e} P_{\eta}(|\beta_{kj}|, \lambda),$$

where P is a scalar penalty function, λ is the penalty tuning constant, and η is a parameter indexing member of a penalty family. Choices of the penalty families include: power family ([Frank and Friedman, 1993](#)), where $P_{\eta}(|x|, \lambda) = \lambda|x|^{\eta}$, $\eta \in (0, 2]$, and in particular lasso ([Tibshirani, 1996](#)) ($\eta = 1$) and ridge ($\eta = 2$); elastic net ([Zou and Hastie, 2005](#)), where $P_{\eta}(|x|, \lambda) = \lambda[(\eta - 1)x^2/2 + (2 - \eta)|x|]$, $\eta \in [1, 2]$; SCAD ([Fan and Li, 2001](#)), where $\partial/\partial|x|P_{\eta}(|x|, \lambda) = \lambda \left\{ \mathbf{1}_{\{|x| \leq \lambda\}} + (\eta\lambda - |x|)_+ / (\eta - 1)\lambda \mathbf{1}_{\{|x| > \lambda\}} \right\}$, $\eta > 2$; and MC+ penalty ([Zhang, 2010](#)), where $P_{\eta}(|x|, \lambda) = \left\{ \lambda|x| - x^2/(2\eta) \right\} \mathbf{1}_{\{|x| < \eta\lambda\}} + 0.5\lambda^2\eta \mathbf{1}_{\{|x| \geq \eta\lambda\}}$. The special case of elastic net for the multinomial-logit model is also implemented in the popular **glmnet** package by [Friedman et al. \(2010\)](#) using coordinate descent algorithm. **MGLM** implements a generic accelerated proximal gradient method that applies to the following two penalties too.

In *groupwise regularization* (penalty='group'),

$$J(\mathbf{B}) = \lambda \sum_{k \in \mathcal{S}} \|\mathbf{B}_{k\cdot}\|_2 = \lambda \sum_{k \in \mathcal{S}} \left(\sum_{j=1}^{d_e} \beta_{kj}^2 \right)^{1/2}.$$

The group penalty ([Yuan and Lin, 2006](#); [Meier et al., 2008](#)) achieves variable selection at the predictor level and leads to a more interpretable model.

Shrinkage and sparsity in terms of the rank of \mathbf{B} is achieved by the *nuclear norm* regularization (penalty='nuclear')

$$J(\mathbf{B}) = \|\mathbf{B}\|_* = \lambda \sum_i \sigma_i(\mathbf{B}),$$

where $\sigma_i(\mathbf{B})$'s are the singular values of the matrix \mathbf{B} . The nuclear norm $\|\mathbf{B}\|_*$ is a suitable convex relaxation of the rank of a matrix parameter. It encourages low rank of the parameter matrix estimate and has been successfully employed in the matrix completion problem (Mazumder et al., 2010), regression with matrix covariates (Zhou and Li, 2014) and predicting at-bat results in baseball (?).

The wrapper function `MGLMtune` facilitates the tuning procedure by performing the regularized estimation over a grid of 30 (default) tuning parameter values using warm start and reports the optimal tuning parameter according to BIC. Users can also supply their own grid points.

Optimization algorithms and implementation

As the DM, NegMN, and GDM distributions do not belong to the exponential family, the usual iteratively reweighted least squares method for maximum likelihood estimation of GLM does *not* apply. The main issue lies in the difficulty of calculating the expected information matrix, which involves evaluating numerous tail probabilities of the marginal distribution (Paul et al., 2005; Zhou and Lange, 2010; Zhou and Zhang, 2012). On the other hand, Newton's method suffers from instability since the log-likelihood functions are non-concave in general.

For distribution fitting, Zhou and Lange (2010) derive stable algorithms based on the minorization-maximization (MM) principle (Lange et al., 2000). Similar to the classical expectation-maximization algorithm, MM algorithm increases the objective value at each iteration and converges to a stationarity point of objective function under mild regularity conditions.

For regression models, Zhang et al. (2017) propose an iteratively reweighted Poisson regression (IRPR) method for maximum likelihood estimation. Their derivation again hinges upon the MM principle, resulting in the much desirable stability of the IRPR algorithm which is critical as the number of parameters is potentially large.

In practice, MM algorithm may suffer from slow convergence especially in the proximity of the optimum. **MGLM** organically combines the MM algorithm and the Newton's method. At each iteration, it computes both MM and Newton updates and chooses the one that results in a higher log-likelihood. Thus, stability is ensured as the log-likelihood always increases. When sufficiently close to the optimum, Newton's method takes over and quickly converges to the MLE in just a few iterations.

An added advantage of the MM algorithm is that it separates parameters and embraces parallel computing (Zhou et al., 2010). Each iteration of the IRPR algorithm involves solving d_e independent Poisson regressions (Zhang et al., 2017) that can be carried out in parallel. Building upon the **parallel** package in R, the `MGLMreg` regression function supports multi-threading on a multi-core machine.

For sparse regression in the `MGLMsparse` function, we implemented the accelerated proximal gradient (Nesterov) method (Zhang et al., 2017). Each iteration only involves evaluation of the gradient of the negative log-likelihood, followed by the elementwise, groupwise, or singular value thresholding according to the regularization being used, and thus scales well with the problem size.

The R package aspect

Three main functions of the **MGLM** package are `MGLMfit` for fitting multivariate distributions, `MGLMreg` for fitting multivariate response regressions, and `MGLMsparse` for fitting sparse regressions. The package adopts S4 object system. In this section, we demonstrate their basic usage using a simulated RNA-seq data set. The R vignette included in the package provides more extensive examples.

The `rnaseq` data that comes with the package is simulated from the **isoform** package (Sun, 2014; Sun et al., 2015) and mimics the real counts generated by the RNA-seq platforms. The simulation mechanism follows the biological process and has nothing to do with the models in Table 1.

In this example, 6 exons are expressed in a gene. Each observation consists of the expression levels (represented by counts) of each exon along with covariates `totalReads`, `treatment`, `gender`, and `age` of an individual. 200 observations are simulated. In the generative model, exon expression levels are affected by intercept, number of total reads (on log scale), and treatment. Age and gender are unrelated to the exon counts.

```
R> library("MGLM")
```

```
R> data("rnaseq")
R> data <- rnaseq[, 1:6]
R> head(rnaseq, n = 3)

      X1 X2 X3 X4 X5 X6 totalReads treatment gender age
1 295 65 19 114 54 20 28317494          0      0 57
2 213 126 12 96 50 4 20015549          0      0 67
3 322 147 23 245 42 19 35318251          0      1 37

R> dim(rnaseq)

[1] 200 10
```

Distribution fitting

We first ignore covariates and demonstrate distribution fitting and model selection with BIC and LRT. The multi-categorical distribution fitting is performed by the function `MGLMfit`.

The primary inputs of the function are the multi-categorical count data in the format of data frame or matrix and the distribution intended to fit. The user can also use the weight argument to specify the weight of each observation. Initial values of the iterative algorithm can also be determined by the user using `init` argument. The function also has `epsilon`, `maxiters`, and `display` to control the convergence threshold, maximum number of iterations to run, and whether to display the result from each iteration, respectively.

The outputs are returned in a list of class "MGLMfit", including parameter estimates, their standard errors, log-likelihood, AIC, BIC, number of iterations to converge. The inversed information matrices and gradients are also returned, but are not printed, in order to keep the printed output concise. When fitting DM and GDM distribution, we also perform LRT, testing against the null hypothesis of using multinomial model. p -values of the LRTs are returned.

The following snippets fit the DM

```
R> system.time (
+   dmFit <- MGLMfit(data, dist = "DM")
+ )
```

```
      user system elapsed
0.255   0.007   0.263
```

```
R> dmFit
```

```
      estimate      SE
alpha_X1 6.128117 0.327888
alpha_X2 2.413647 0.139676
alpha_X3 1.625627 0.099424
alpha_X4 6.822929 0.362568
alpha_X5 2.214236 0.129233
alpha_X6 0.784028 0.051369
```

```
Distribution: Dirichlet Multinomial
Log-likelihood: -4968.666
BIC: 9969.121
AIC: 9949.331
LRT test p value: <0.0001
Iterations: 6
```

and the GDM model

```
R> system.time(
+   gdmFit <- MGLMfit(data, dist = "GDM")
+ )
```

```
      user system elapsed
0.380   0.019   0.399
```

```
R> gdmFit
```

	estimate	SE
alpha_X1	3.741846	0.367088
alpha_X2	2.400909	0.815431
alpha_X3	1.558396	0.233136
alpha_X4	6.988354	1.164764
alpha_X5	20.689398	0.149279
beta_X1	8.026379	0.966502
beta_X2	11.038376	0.725978
beta_X3	8.961428	0.264520
beta_X4	2.702723	2.871718
beta_X5	4.854816	0.648271

Distribution: Generalized Dirichlet Multinomial
 Log-likelihood: -4841.231
 BIC: 9735.446
 AIC: 9702.463
 LRT test p value: <0.0001
 Iterations: 59

Both `dmFit` and `gdmFit` give the LRT p -value for comparing the fitted model with the MN model. In this example, both are significantly better than MN, with p -values $\ll 0.05$. To compare DM and GDM, we can either compare their BICs or perform a formal LRT.

```
R> LRT <- -2 * (logLik(dmFit) - logLik(gdmFit))
R> pchisq(LRT, ncol(data) - 2, lower.tail = FALSE)

[1] 5.817352e-54
```

Both suggest that GDM provides a significantly better fit than DM.

The NegMN model

```
R> system.time(
+   negmnFit <- MGLMfit(data, dist = "NegMN")
+ )
```

user	system	elapsed
0.006	0.002	0.009

```
R> print(negmnFit)
```

	estimate	SE
p_X1	0.311486	0.001362
p_X2	0.106491	0.000850
p_X3	0.098373	0.000819
p_X4	0.350496	0.001425
p_X5	0.094263	0.000803
p_X6	0.021220	0.000389
phi	12.232569	1.229253

Distribution: Negative Multinomial
 Log-likelihood: -20673.71
 BIC: 41384.52
 AIC: 41361.43
 LRT test p value:
 Iterations: 3

yields a much larger BIC than those of DM and GDM. LRT does not apply here, since NegMN is not a sub-model of the other three.

Regression

The more interesting question is whether the covariates have a significant relationship to the responses. Regressions are performed using function `MGLMreg`. First, the regression formula is required by the `MGLMreg` function. When specifying the regression formula, the response matrix is on the left hand side and the covariates on the right, following the convention in `lm` and `glm`. The model is specified

using the `dist` argument. The input argument `data` is optional. When specified, the formula is built based on the supplied data frame; otherwise, the function searches through the global environment for the data elements. Similar to the distribution fitting function, weights of the observations can be specified by the `weight` argument, and initial values can be supplied using `init` arguments. Parallel computing is also implemented in the package. Setting `parallel=TRUE` and giving the number of cores using the argument `core` invokes multi-threading. The other arguments used to control the algorithm convergence and display include `epsilon`, `maxiters`, `display`, and `LRT`.

The output of `MGLMreg` is a list of class "MGLMreg", containing the estimated regression coefficients, their standard errors, Wald test statistics and their corresponding p -values for each predictor, log-likelihood, AIC, BIC, gradient and Hessian matrix at the estimate, number of iterations, and fitted values.

We fit the four regression models in Table 1 with all 5 covariates: intercept, number of total reads (on log scale), treatment, age, and gender.

A few observations can be made from the following output. BIC indicates the GDM model as the best fit, followed by the DM model. This is consistent with the distribution fitting results. Note that the hypothesis testing results in the four models are different. In the MN model, all covariates are significant; however, this is not true because age and gender have no effects in the generative model. DM also wrongly identifies age as a significant predictor. Only the GDM model correctly identifies true significant predictors.

MN regression

```
R> system.time(
+   mnreg <- MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
+     treatment + age + gender, data = rnaseq, dist = "MN")
+ )
```

```
      user  system elapsed
0.142    0.006    0.149
```

```
R> print(mnreg)
```

```
Call: MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
  treatment + age + gender, data = rnaseq, dist = "MN")
```

Coefficients:

	X1	X2	X3	X4	X5
[1,]	4.942732	5.009649	-3.792216	4.435434	4.027689
[2,]	-0.112845	-0.170222	0.219277	-0.107260	-0.120928
[3,]	-0.022655	-0.043099	2.745277	1.405742	0.092246
[4,]	-0.006187	-0.009709	-0.005907	-0.010945	-0.009599
[5,]	0.032676	0.100389	0.020663	0.103859	0.009514

Hypothesis test:

	wald value	Pr(>wald)
(Intercept)	144.88789	1.634268e-29
log(totalReads)	69.92572	1.061922e-13
treatment	18364.13260	0.000000e+00
age	79.91023	8.762650e-16
gender	52.33670	4.601575e-10

Distribution: Multinomial

Log-likelihood: -7506.393

BIC: 15145.24

AIC: 15062.79

Iterations: 6

DM regression

```
R> system.time(
+   dmreg <- MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
+     treatment + age + gender, data = rnaseq, dist = "DM")
+ )
```

```

      user system elapsed
      0.182  0.004  0.187

R> print(dmreg)

Call: MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
  treatment + age + gender, data = rnaseq, dist = "DM")

Coefficients:
           X1           X2           X3           X4           X5           X6
[1,] -0.895850 -1.096921 -8.997414 -1.736871 -1.774227 -5.646822
[2,]  0.221988  0.186919  0.536572  0.252679  0.216672  0.347271
[3,] -0.679291 -0.686881  1.835585  0.707954 -0.546469 -0.543134
[4,]  0.010245  0.005227  0.009134  0.004252  0.006090  0.011642
[5,] -0.026177  0.040244 -0.052842  0.023178 -0.058339 -0.039139

Hypothesis test:
                wald value Pr(>wald)
(Intercept)      14.579069  0.023796
log(totalReads)   8.502549  0.203547
treatment      1851.437449  0.000000
age              13.131512  0.040994
gender           4.133364  0.658634

Distribution: Dirichlet Multinomial
Log-likelihood: -4386.941
BIC: 8932.831
AIC: 8833.882
Iterations: 9

```

GDM regression

```

R> system.time(
+   gdmreg <- MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
+   treatment + age + gender, data = rnaseq, dist = "GDM")
+ )

      user system elapsed
      0.219  0.003  0.224

R> print(gdmreg)

Call: MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
  treatment + age + gender, data = rnaseq, dist = "GDM")

Coefficients:
      alpha_X4 alpha_X1 alpha_X2 alpha_X3 alpha_X5 beta_X4
[1,]  5.987993 -7.056673  0.456088 -10.120738  2.639396  4.661089
[2,] -0.215099  0.555973  0.039553  0.720358 -0.016121 -0.140896
[3,] -0.047691 -0.329320  0.979359  0.099958  0.063393  0.628878
[4,]  0.006661 -0.004343  0.019361  0.008173  0.012397  0.003224
[5,]  0.233006  0.374838 -0.186420 -0.202417  0.144289  0.212071
      beta_X1 beta_X2 beta_X3 beta_X5
[1,] -9.789127  7.095061 -9.530008 -1.687615
[2,]  0.713819 -0.222984  0.743146  0.133985
[3,]  0.746198 -1.591630 -0.923712 -0.042441
[4,]  0.000453  0.015945  0.012541  0.019188
[5,]  0.273256 -0.233121 -0.270428  0.122062

Hypothesis test:
                wald value Pr(>wald)
(Intercept)      15.40109  0.118109
log(totalReads)  11.04187  0.354265
treatment      2549.23829  0.000000
age              16.42846  0.088007

```

```
gender          10.72122  0.379646
```

```
Distribution: Generalized Dirichlet Multinomial
Log-likelihood: -4289.281
BIC: 8843.479
AIC: 8678.563
Iterations: 46
```

NegMN regression

There are two variants of NegMN regression, depending on whether to link over-dispersion parameter to covariates. The default setting `regBeta=FALSE` instructs `MGLMreg` to fit the NegMN regression with all observations sharing the same over-dispersion parameter value. There are $pd + 1$ parameters.

```
R> system.time(
+   negmreg2 <- MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~
+     log(totalReads) + treatment + age + gender,
+     data = rnaseq, dist = "NegMN", regBeta = FALSE)
+ )
```

```
user system elapsed
0.196  0.004  0.201
```

```
R> print(negmreg2)
```

```
Call: MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
  treatment + age + gender, data = rnaseq, dist = "NegMN",
  regBeta = FALSE)
```

Coefficients:

\$alpha

	X1	X2	X3	X4
(Intercept)	-13.587385	-13.521818	-22.380101	-14.131348
log(totalReads)	0.907716	0.850412	1.242922	0.915258
treatment	-0.753113	-0.773507	2.014641	0.675195
age	0.002583	-0.000938	0.002916	-0.002141
gender	-0.060696	0.007022	-0.069502	0.012499

	X5	X6
(Intercept)	-14.507698	-18.526425
log(totalReads)	0.899918	1.020360
treatment	-0.638296	-0.730410
age	-0.000824	0.008766
gender	-0.083681	-0.093397

\$phi

```
phi
31.6062
```

Hypothesis test:

	wald value	Pr(>wald)
(Intercept)	385.75540	3.223413e-80
log(totalReads)	368.08485	2.017976e-76
treatment	18377.52958	0.000000e+00
age	79.70906	4.103065e-15
gender	54.84662	4.978098e-10

Distribution: Negative Multinomial

```
Log-likelihood: -8746.689
BIC: 17657.63
AIC: 17555.38
Iterations: 35
```

`regBeta=TRUE` instructs `MGLMreg` to link over-dispersion parameter to covariates and there are $p(d + 1)$ regression coefficients. Small likelihood, larger AIC/BIC and slow convergence reflects the lack of fit of this model.

```
R> system.time(
+   negmnreg <- MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~
+     log(totalReads) + treatment + age + gender,
+     data = rnaseq, dist = "NegMN", regBeta = TRUE)
+ )

   user  system elapsed
 9.866   0.023   9.898

R> print(negmnreg)

Call: MGLMreg(formula = cbind(X1, X2, X3, X4, X5, X6) ~ log(totalReads) +
  treatment + age + gender, data = rnaseq, dist = "NegMN",
  regBeta = TRUE)

Coefficients:
              X1          X2          X3          X4
(Intercept) -17.648355 -17.582555 -26.462109 -18.204282
log(totalReads)  1.192057  1.134742  1.528500  1.200309
treatment      -0.877324 -0.897715  1.890375  0.550944
age             -0.013397 -0.016918 -0.013072 -0.018127
gender         -0.101456 -0.033730 -0.110253 -0.028252
              X5          X6          phi
(Intercept) -18.569609 -22.587821  7.543157
log(totalReads)  1.184315  1.304725 -0.285737
treatment      -0.762503 -0.854624  0.125412
age             -0.016804 -0.007213  0.015871
gender         -0.124433 -0.134173  0.041254

Hypothesis test:
           wald value    Pr(>wald)
(Intercept)    291.48017 3.987668e-59
log(totalReads) 371.39226 3.232075e-76
treatment    18377.18774 0.000000e+00
age           81.70350 6.187095e-15
gender       54.79955 1.633654e-09

Distribution: Negative Multinomial
Log-likelihood: -8745.162
BIC: 17675.77
AIC: 17560.32
Iterations: 140
```

Sparse regression

The function `MGLMsparsereg` performs regularized estimation. Similar to `MGLMreg`, the inputs of the sparse regression function include `formula`, `data`, `dist`, and the convergence controlling arguments. The function also requires the tuning parameter `lambda`, and the penalty type argument `penalty`. The outputs include the coefficient estimates, log-likelihood, AIC, BIC, degrees of freedom, and the number of iterations.

We simulate 100 data points from a 5-variate DM model using 10 covariates. Only three of them (1, 3, and 5) have non-zero effects. For each 5-variate data point, batch size, or the total number of objects that are put into 5 categories, is drawn from $Bin(200, 0.8)$.

```
R> dist <- "DM"
R> n <- 100
R> p <- 10
R> d <- 5
R> set.seed(118)
R> m <- rbinom(n, 200, 0.8)
R> X <- matrix(rnorm(n * p), n, p)
R> alpha <- matrix(0, p, d)
R> alpha[c(1, 3, 5), ] <- 1
R> Alpha <- exp(X %*% alpha)
```

```

R> Y <- rdirnm(size = m, alpha = Alpha)
R> length(m)

[1] 100

R> head(m)

[1] 167 160 162 159 156 157

R> head(Y)

      [,1] [,2] [,3] [,4] [,5]
[1,]   24    7  112   15    9
[2,]   34   33   31   38   24
[3,]    0    0    0    0  162
[4,]    7   17   84   29   22
[5,]    0   33    0  123    0
[6,]    0    0    3  154    0

R> head(rowSums(Y))

[1] 167 160 162 159 156 157

```

We demonstrate the regularized estimation by group, nuclear norm, and element-wise penalization.

Variable selection by group penalty

With input $\lambda = \text{Inf}$, `MGLMsparsereg` returns λ_{\max} , the maximum value the tuning parameter can take such that not all regression coefficient estimates are 0.

```

R> pen <- "group"
R> ngridpt <- 30
R> spmodelfit <- MGLMsparsereg(formula = Y ~ 0 + X, dist = dist,
+                             lambda = Inf, penalty = pen)
R> maxlambda <- maxlambda(spmodelfit)
R> lambdas <- exp(seq(from = log(maxlambda), to = log(maxlambda / nrow(Y)),
+                    length.out = ngridpt))

```

Tuning is performed on 30 grid points. The left panel of Figure 1 displays the BIC trace along the solution path.

```

R> BICs <- rep(0, ngridpt)
R> AICs <- rep(0, ngridpt)
R> LogLs <- rep(0, ngridpt)
R> Dofs <- rep(0, ngridpt)
R> ptm <- proc.time()
R> for (j in 1:ngridpt) {
+   if (j == 1) {
+     B0 <- matrix(0, p, ncol(coef(spmodelfit)))
+   }
+   else B0 <- B_hat
+   select.fit <- MGLMsparsereg(formula = Y ~ 0 + X, dist = dist,
+                               lambda = lambdas[j], penalty = pen, init = B0)
+   B_hat <- coef(select.fit)
+   BICs[j] <- BIC(select.fit)
+   LogLs[j] <- logLik(select.fit)
+   AICs[j] <- AIC(select.fit)
+   Dofs[j] <- dof(select.fit)
+ }
R> proc.time() - ptm

      user  system elapsed
 4.469   0.026   4.500

R> pen <- "group"
R> ngridpt <- 30

```

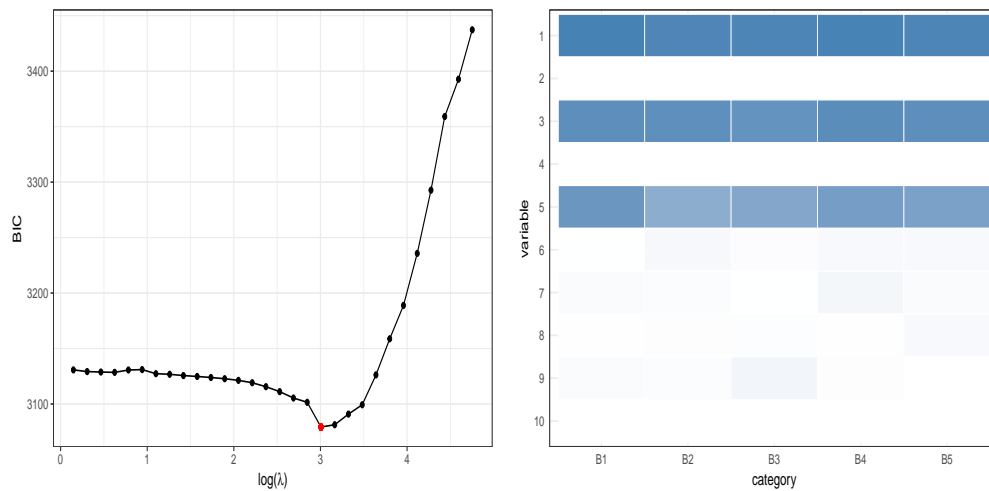


Figure 1: Variable selection by the group penalty. Left: BIC trace. Right: Regularized estimate $\widehat{B}(\lambda)$ at the optimal λ displayed in gray scale.

```
R> smodelfit <- MGLMsparereg(formula = Y ~ 0 + X, dist = dist,
+                           lambda = Inf, penalty = pen)
R> maxlambda <- maxlambda(smodelfit)
R> lambdas <- exp(seq(from = log(maxlambda), to = log(maxlambda / nrow(Y)),
+                   length.out = ngridpt))
```

The right panel of Figure 1 displays the regularized estimate $\widehat{B}(\lambda)$ at the tuning parameter value with minimal BIC.

```
R> chosen.lambda <- lambdas[which.min(BICs)]
R> select <- MGLMsparereg(formula = Y ~ 0 + X, dist = dist,
+                       lambda = chosen.lambda, penalty = pen)
```

Alternatively, the function `MGLMtune` automates the tuning procedure and reports the regularized estimate at the optimal tuning parameter value according to BIC.

```
R> selectTune <- MGLMtune(Y ~ 0 + X, dist = dist, penalty = pen, ngridpt = 30,
+                       display = FALSE)
```

The option `ngridpt` sets the number of grid points n_{grid} and the sequence of tuning parameters is equally spaced on the log scale within the interval $[\lambda_{\text{max}}/n_{\text{grid}}, \lambda_{\text{max}}]$.

Low rank regression by nuclear norm regularization

Nuclear norm regularization is invoked by setting `penalty="nuclear"`.

```
R> system.time (
+   select <- MGLMtune(Y ~ 0 + X, dist = "DM", penalty = "nuclear",
+                   ngridpt = 30, display = FALSE))
```

```
   user  system elapsed
 4.475   0.037   4.528
```

Figure 2 displays the BIC trace plot and the regularized estimate at optimal λ from the same data by the nuclear norm penalty.

Select by entries

```
R> system.time (
+   select <- MGLMtune(Y ~ 0 + X, dist = "DM", penalty = "sweep", ngridpt = 30,
+                   display = FALSE))
```

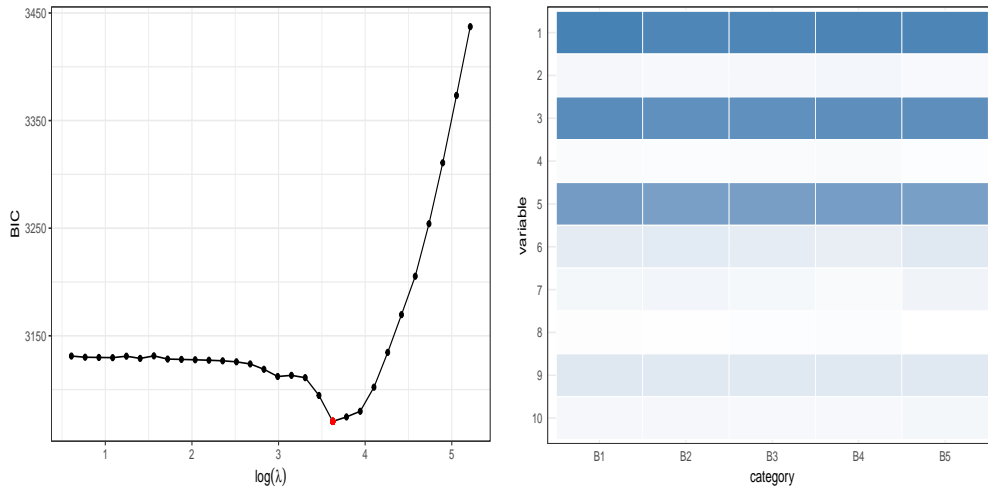


Figure 2: Low rank regression by the nuclear norm penalty. Left: BIC trace. Right: Regularized estimate $\hat{B}(\lambda)$ at the optimal λ displayed in gray scale.

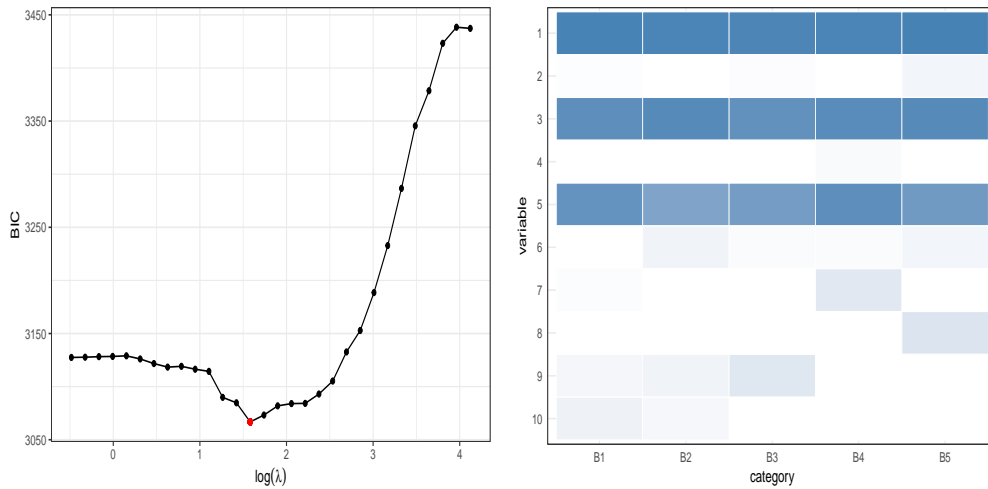


Figure 3: Select by parameter matrix entries with L1 norm penalty. Left: BIC trace. Right: Regularized estimate $\hat{B}(\lambda)$ at the optimal λ displayed in gray scale.

```

user  system elapsed
4.448  0.038  4.504
    
```

Figure 3 displays the BIC trace plot and the regularized estimate at optimal λ from the same data by the element-wise lasso penalty.

Discussion

This article introduces the **MGLM** package for analysis of multivariate categorical data. Distribution fitting, regression, sparse regression, and random number generation are implemented in a simple and unified framework. It timely responds to the current challenge of multivariate categorical data analysis arising from modern technology such as RNA-seq. The R package is available on CRAN.

There are several possible extensions that would be useful to the package. Some of them include:

1. Alternative parameterization. Some models in Table 1 admits alternative parameterization. For

instance, the DM distribution can be re-parameterized as

$$\theta = \frac{1}{\sum_j \alpha_j}, \quad p_j = \frac{\alpha_j}{\sum_{j'} \alpha_{j'}}, \quad j = 1, \dots, d.$$

in terms of the proportion vector $\mathbf{p} = (p_1, \dots, p_d) \in \Delta_d$ and the overdispersion parameter $\theta > 0$. Appropriate inverse link function can be

$$p_j = \frac{e^{\mathbf{x}^T \boldsymbol{\beta}_j}}{1 + \sum_{j'=1}^{d-1} e^{\mathbf{x}^T \boldsymbol{\beta}_{j'}}}, \quad j = 1, \dots, d-1,$$

$$\theta = e^{\mathbf{x}^T \boldsymbol{\beta}_d}.$$

The multinomial-logit model can be treated as a special case with $\boldsymbol{\beta}_d = \mathbf{0}$. Zhou and Lange (2010) discuss an algorithm for distribution fitting using this parameterization. Corresponding estimation algorithm for the regression model needs to be devised and implemented. Similar re-parameterization applies to the GDM model.

2. Alternative link function. Current version only implements the log link function for positive distribution parameter and logit link for the probability vector. Inclusion of alternative link functions such as probit and cloglog would expand the flexibility of the models.
3. Ordinal categorical responses. Multinomial-logit model can be adapted to ordinal categorical responses (Agresti, 2002, Chapter 7). Parallel developments and implementation for the DM, NegMN, and GDM models are worth considering.
4. Parameter constraints. Current version does not allow constraints among regression parameters. MGLMreg calls `glm.fit` functions to fit weighted Poisson regressions in each iteration; we may call functions from `glm` package (Chaudhuri et al., 2006) instead to incorporate parameter constraints.
5. The `xij` argument (Yee, 2015, Chapter 14). Current version assumes the same set of covariates for all categories. Allowing covariates to take different values for each category can be useful, e.g., for discrete choice modeling in econometrics. The corresponding algorithm and implementation are worth exploring.

The MGLM package for R is continually being developed.

Acknowledgments

The work is partially supported by NSF grants DMS-1127914, DMS-1310319 and NIH grants HG006139, GM105785 and GM53275.

Bibliography

- A. Agresti. *Categorical Data Analysis*. Wiley Series in Probability and Statistics. John Wiley & Sons, New York, 2nd edition, 2002. ISBN 0-471-36093-7. [p1, 16]
- S. G. Baker. The multinomial-poisson transformation. *Journal of the Royal Statistical Society. Series D (The Statistician)*, 43(4):pp. 495–504, 1994. ISSN 00390526. URL <http://www.jstor.org/stable/2348134>. [p2]
- N. Bouguila. Clustering of count data using generalized dirichlet multinomial distributions. *IEEE Transactions on Knowledge and Data Engineering*, 20(4):462–474, 2008. ISSN 1041-4347. URL <http://doi.org/10.1109/TKDE.2007.190726>. [p4]
- S. Boyd and L. Vandenberghe. *Convex Optimization*. Cambridge University Press, Cambridge, 2004. ISBN 0-521-83378-7. [p2]
- S. Chaudhuri, M. S. Handcock, and M. S. Rendall. *glm: An R Package for Generalized Linear Models Subject to Constraints*, 2006. URL <http://www.stat.washington.edu/handcock/combining>. [p16]
- R. J. Connor and J. E. Mosimann. Concepts of independence for proportions with a generalization of the Dirichlet distribution. *J. Amer. Statist. Assoc.*, 64:194–206, 1969. ISSN 0162-1459. [p4]
- B. Efron and D. V. Hinkley. Assessing the accuracy of the maximum likelihood estimator: Observed versus expected Fisher information. *Biometrika*, 65(3):457–487, 1978. ISSN 0006-3444. URL <http://doi.org/10.1093/biomet/65.3.457>. [p5]

- J. Fan and R. Li. Variable selection via nonconcave penalized likelihood and its oracle properties. *J. Amer. Statist. Assoc.*, 96(456):1348–1360, 2001. ISSN 0162-1459. URL <http://doi.org/10.1198/016214501753382273>. [p5]
- I. E. Frank and J. H. Friedman. A statistical view of some chemometrics regression tools. *Technometrics*, 35(2):109–135, 1993. ISSN 00401706. URL <http://doi.org/10.2307/1269656>. [p5]
- J. H. Friedman, T. Hastie, and R. Tibshirani. Regularization paths for generalized linear models via coordinate descent. *Journal of Statistical Software*, 33(1):1–22, 2010. ISSN 1548-7660. URL <http://www.jstatsoft.org/v33/i01>. [p1, 5]
- R. L. Graham, D. E. Knuth, and O. Patashnik. *Concrete Mathematics*. Addison-Wesley Publishing Company, Reading, MA, 2nd edition, 1994. ISBN 0-201-55802-5. A foundation for computer science. [p3]
- J. B. Lang. On the comparison of multinomial and Poisson log-linear models. *J. Roy. Statist. Soc. Ser. B*, 58(1):253–266, 1996. ISSN 0035-9246. URL [http://links.jstor.org/sici?sici=0035-9246\(1996\)58:1<253:OTCOMA>2.0.CO;2-P&origin=MSN](http://links.jstor.org/sici?sici=0035-9246(1996)58:1<253:OTCOMA>2.0.CO;2-P&origin=MSN). [p2]
- K. Lange, D. R. Hunter, and I. Yang. Optimization transfer using surrogate objective functions. *J. Comput. Graph. Statist.*, 9(1):1–59, 2000. ISSN 1061-8600. With discussion, and a rejoinder by Hunter and Lange. [p6]
- R. Mazumder, T. Hastie, and R. Tibshirani. Spectral regularization algorithms for learning large incomplete matrices. *Journal of Machine Learning Research*, 11:2287–2322, 2010. [p6]
- L. Meier, S. van de Geer, and P. Bühlmann. The group Lasso for logistic regression. *J. R. Stat. Soc. Ser. B Stat. Methodol.*, 70(1):53–71, 2008. ISSN 1369-7412. [p5]
- S. R. Paul, U. Balasooriya, and T. Banerjee. Fisher information matrix of the Dirichlet-multinomial distribution. *Biom. J.*, 47(2):230–236, 2005. ISSN 0323-3847. [p6]
- W. Sun. *Isoform: A Set of Tools for RNA Isoform Study Using RNA-Seq Data*, 2014. URL <http://www.bios.unc.edu/~weisun/software/isoform.htm>. R package version 0.99.2. [p6]
- W. Sun, Y. Liu, J. J. Crowley, and et al. IsoDOT detects differential RNA-isoform expression/usage with respect to a categorical or continuous covariate with high sensitivity and specificity. *J. Amer. Statist. Assoc.*, 110(511):975–986, 2015. ISSN 0162-1459. URL <http://doi.org/10.1080/01621459.2015.1040880>. [p6]
- R. Tibshirani. Regression shrinkage and selection via the lasso. *J. Roy. Statist. Soc. Ser. B*, 58(1):267–288, 1996. ISSN 0035-9246. URL [http://links.jstor.org/sici?sici=0035-9246\(1996\)58:1<267:RSASVT>2.0.CO;2-G&origin=MSN](http://links.jstor.org/sici?sici=0035-9246(1996)58:1<267:RSASVT>2.0.CO;2-G&origin=MSN). [p5]
- T. Tvedebrink. Overdispersion in allelic counts and θ -correction in forensic genetics. *Theoretical Population Biology*, 78(3):200–210, 2010. ISSN 0040-5809. URL <http://doi.org/10.1016/j.tpb.2010.07.002>. [p1]
- W. N. Venables and B. D. Ripley. *Modern Applied Statistics with S*. Springer-Verlag, New York, 4th edition, 2002. ISBN 0-387-95457-0. URL <http://www.stats.ox.ac.uk/pub/MASS4>. [p1]
- T. W. Yee. The VGAM package for categorical data analysis. *Journal of Statistical Software*, 32(10):1–34, 2010. ISSN 1548-7660. URL <http://www.jstatsoft.org/v32/i10>. [p1]
- T. W. Yee. *Vector Generalized Linear and Additive Models: With an Implementation in R*. Springer-Verlag, New York, USA, 2015. [p1, 16]
- T. W. Yee. *VGAM: Vector Generalized Linear and Additive Models*, 2017. URL <https://CRAN.R-project.org/package=VGAM>. R package version 1.0-4. [p1]
- M. Yuan and Y. Lin. Model selection and estimation in regression with grouped variables. *J. R. Stat. Soc. Ser. B Stat. Methodol.*, 68(1):49–67, 2006. ISSN 1369-7412. URL <http://doi.org/10.1111/j.1467-9868.2005.00532.x>. [p5]
- C.-H. Zhang. Nearly unbiased variable selection under minimax concave penalty. *Ann. Statist.*, 38(2): 894–942, 2010. ISSN 0090-5364. URL <http://doi.org/10.1214/09-AOS729>. [p5]
- Y. Zhang, H. Zhou, J. Zhou, and W. Sun. Regression models for multivariate count data. *J. Comput. Graph. Statist.*, 26(1):1–13, 2017. ISSN 1061-8600. URL <http://doi.org/10.1080/10618600.2016.1154063>. [p6]

- H. Zhou and K. L. Lange. MM algorithms for some discrete multivariate distributions. *Journal of Computational and Graphical Statistics*, 19:645–665, 2010. [p4, 6, 16]
- H. Zhou and L. Li. Regularized matrix regressions. *Journal of Royal Statistical Society, Series B*, 76(2): 463–483, 2014. [p6]
- H. Zhou and Y. Zhang. EM vs MM: a case study. *Computational Statistics & Data Analysis*, 56:3909–3920, 2012. [p6]
- H. Zhou, K. L. Lange, and M. A. Suchard. Graphical processing units and high-dimensional optimization. *Statistical Science*, 25:311–324, 2010. [p6]
- H. Zou and T. Hastie. Regularization and variable selection via the elastic net. *J. R. Stat. Soc. Ser. B Stat. Methodol.*, 67(2):301–320, 2005. ISSN 1369-7412. URL <http://doi.org/10.1111/j.1467-9868.2005.00503.x>. [p5]

Juhyun Kim
Department of Biostatistics
University of California, Los Angeles
juhkim111@ucla.edu

Yiwen Zhang
KPMG LLP
Irvine, CA
zhangyiwen1015@gmail.com

Joshua Day
Department of Statistics
North Carolina State University
jtday2@ncsu.edu

Hua Zhou
Department of Biostatistics
University of California, Los Angeles
huazhou@ucla.edu